1. NAME OF THE MEDICINAL PRODUCT

Esperoct® 1000 IU

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Esperoct 1000 IU powder and solvent for solution for injection
Each powder vial contains nominally 1000 IU turoctocog alfa pegol*.
After reconstitution, 1 mL of solution contains approximately 250 IU turoctocog alfa pegol.

*Human factor VIII, produced by recombinant DNA technology in a Chinese Hamster Ovary (CHO) cell line, and no additives of human or animal origin are used in the cell culture, purification, conjugation or formulation of Esperoct.

Excipient with known effect

Each reconstituted vial contains 30.5 mg of sodium (see section 4.4).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

The powder is white to off-white.

The solvent is clear and colourless.

pH: 6.9.

Osmolality: 590 mOsmol/kg.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment and prophylaxis of haemorrhages in previously treated patients with haemophilia A (congenital factor VIII disorder).

Esperoct does not contain any pharmacologically active quantities of the Von Willebrand factor and is therefore not suitable for the treatment of von Willebrand's disease.

4.2 Posology and method of administration

Treatment should be initiated under the supervision of a physician experienced in the treatment of haemophilia.

Previously untreated patients

The safety and efficacy of Esperoct in previously untreated patients have not yet been established.

Treatment monitoring

During the course of treatment, appropriate determination of factor VIII activity levels is advised to guide adjustments of the dosing regimen of Esperoct, if needed. Individual patients may vary in their response to factor VIII, demonstrating different half-lives and incremental recoveries. Dose based on bodyweight may require adjustment in underweight or overweight patients. In the case of major surgical interventions in particular, monitoring of the factor VIII substitution therapy by measurement of plasma factor VIII activity is necessary.

The factor VIII activity of Esperoct can be measured using the conventional factor VIII assays, the chromogenic assay and the one-stage assay.
When using an in vitro thromboplastin time (aPTT)-based one stage clotting assay for determining factor VIII activity in patients' blood samples, plasma factor VIII activity results can be significantly affected by both the type of aPTT reagent and the reference standard used in the assay.
When using a one-stage clotting assay some silica based reagents should be avoided as they cause underestimation. Also there can be significant discrepancies between assay results obtained by aPTT based one stage clotting assay and the chromogenic assay according to Ph. Eur. This is of importance particularly when changing the laboratory and/or reagents used in the assay.

Posology

The dose, dosing interval and duration of the substitution therapy depend on the severity of the factor VIII deficiency, on the location and extent of the bleeding, on the targeted factor VIII activity level and the patient's clinical condition. The number of units of factor VIII administered is expressed in International Units (IU), which is related to the current WHO concentrate standard for factor VIII products. The activity of factor VIII in plasma is expressed either as percentage (relative to normal human plasma level) or in International Units per dL (relative to the current International Standard for factor VIII in plasma).

One International Unit (IU) of factor VIII activity is equivalent to that quantity of factor VIII in one ml of human plasma.

On demand treatment and treatment of bleeding episodes

The calculation of the required dose of factor VIII is based on the empirical finding that 1 International Unit (IU) factor VIII per kg body weight raises the plasma factor VIII activity by 2 IU/dL.

The required dose is determined using the following formula:
Required units (IU) = body weight (kg) x desired factor VIII rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL).

The amount to be administered and the frequency of administration should always be oriented to the clinical effectiveness in the individual case.

Guidance for the dosing of Esperoct for the on-demand treatment and treatment of bleeding episodes is provided in table 1. Plasma factor VIII activity levels should be maintained at or above the described plasma levels (in IU per dL or % of normal). For treatment of bleeds a

maximum single dose of Esperoct at 75 IU/kg and a maximum total dose of 200 IU/kg/24 hours may be administered.

Table 1 Guidance for treatment of bleeding episodes with Esperoct

Degree of haemorrhage	Factor VIII level required (IU/dL or % of normal)[a]	Frequency of doses (hours)	Duration of therapy
Mild Early haemarthrosis, mild muscle bleeding or mild oral bleeding	20-40	12-24	Until the bleeding is resolved
Moderate More extensive haemarthrosis, muscle bleeding, haematoma	30-60	12-24	Until the bleeding is resolved
Severe or life-threatening haemorrhages	60-100	8-24	Until the threat is resolved

[a] The required dose is determined using the following formula:
Required units (IU) = body weight (kg) x desired factor VIII rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL).

Perioperative management

The dose level and dosing intervals for surgery depend on the procedure and local practice. A maximum single dose of Esperoct at 75 IU/kg and a maximum total dose of 200 IU/kg/24 hours may be administered.
The frequency of doses and duration of therapy should always be individually adjusted based on individual clinical response.

Table 2 includes general recommendation for dosing of Esperoct for perioperative management.
Consideration should be given to maintain a factor VIII activity at or above the target range.

Table 2 Guidance for dosing of Esperoct for perioperative management

Type of surgical procedure	Factor VIII level required (%) (IU/dL)[a]	Frequency of doses (hours)	Duration of therapy
Minor surgery Including tooth extraction	30-60	Within one hour before surgery Repeat after 24 hours if necessary	Single dose or repeat injection every 24 hours for at least 1 day until healing is achieved
Major surgery	80-100 (pre- and post-operative)	Within one hour before surgery to achieve factor VIII activity within the target range Repeat every 8 to 24 hours to maintain factor VIII activity within the target range	Repeat injection every 8 to 24 hours as necessary until adequate wound healing is achieved Consider to continue therapy for another 7 days to maintain a

			factor VIII activity of 30% to 60% (IU/dL)

[a] The required dose is determined using the following formula:
Required units (IU) = body weight (kg) x desired factor VIII rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL).

Prophylaxis
Adults and adolescents (age 12 and over): The recommended dose is 50 IU of Esperoct per kg body weight every 4 days.

Adjustments of doses and administration intervals may be considered based on achieved factor VIII levels and individual bleeding tendency.

Paediatric population
The dose in adolescents (12 years and above) is the same as for adults.

Children (under 12): One dose of 65 IU (50-75 IU) Esperoct® per kg body weight is administered twice a week.

Method of administration

Esperoct is for intravenous use.

Esperoct should be administered by intravenous injection (over approximately 2 minutes) after reconstitution of the powder with 4 mL supplied solvent (sodium chloride 9 mg/mL (0.9%) solution for injection).

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Known allergic reaction to hamster protein.

4.4 Special warnings and precautions for use

Traceability

In order to improve traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity

Allergic-type hypersensitivity reactions are possible with Esperoct. The product contains traces of hamster proteins, which in some patients may cause allergic reactions. If symptoms of hypersensitivity occur, patients should be advised to immediately discontinue the use of the medicinal product and contact their physician. Patients should be informed of the early signs of hypersensitivity reactions including hives, generalised urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis.

In case of shock, standard medical treatment for shock should be implemented.

Inhibitors

The formation of neutralising antibodies (inhibitors) to factor VIII is a known complication in the management of individuals with haemophilia A. These inhibitors are usually IgG immunoglobulins directed against the factor VIII pro-coagulant activity, which are quantified in Bethesda Units (BU) per ml of plasma using the modified assay. The risk of developing inhibitors is correlated to the severity of the disease as well as the exposure to factor VIII, this risk being highest within the first 50 exposure days but continues throughout life although the risk is uncommon.

The clinical relevance of inhibitor development will depend on the titre of the inhibitor, with low titre posing less of a risk of insufficient clinical response than high titre inhibitors.
In general, all patients treated with coagulation factor VIII products should be carefully monitored for the development of inhibitors by appropriate clinical observations and laboratory tests. If the expected factor VIII activity plasma levels are not attained, or if bleeding is not controlled with an appropriate dose, testing for factor VIII inhibitor presence should be performed. In patients with high levels of inhibitor, factor VIII therapy may not be effective and other therapeutic options should be considered.
Management of such patients should be directed by physicians with experience in the care of haemophilia and factor VIII inhibitors.

Decreased factor VIII activity in previously treated patients

From post marketing reports, a decreased factor VIII activity in the absence of detectable factor VIII inhibitors has been reported in previously treated patients. The decreased factor VIII activity was observed at time of switching to Esperoct and may, in some cases, have been associated with anti-PEG antibodies. Appropriate determination of factor VIII activity upon switching should be considered.
See section 4.8 for additional information.

Cardiovascular events

In patients with existing cardiovascular risk factors, substitution therapy with factor VIII may increase the cardiovascular risk.

Catheter-related complications

If a central venous access device (CVAD) is required, the risk of CVAD-related complications including local infections, bacteraemia and catheter site thrombosis should be considered.

Paediatric population

The listed warnings and precautions apply to adults, adolescents (12-18 years) and children (under 12 years).

Excipient-related considerations

The medicinal product contains 30.5 mg sodium per reconstituted vial, equivalent to 1.5% of the WHO recommended maximum daily intake of 2.0 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions of human coagulation factor VIII (rDNA) with other medicinal products have been reported.

4.6 Fertility, pregnancy and lactation

Animal reproduction studies have not been conducted with factor VIII. Based on the rare occurrence of haemophilia A in women, experience regarding the use of factor VIII during pregnancy and breast-feeding is not available. Therefore, factor VIII should be used during pregnancy and lactation only if clearly indicated.

4.7 Effects on ability to drive and use machines

Esperoct has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the infusion site, chills, flushing, generalised urticaria, headache, hives, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) have been observed rarely and may in some cases progress to severe anaphylaxis (including shock).

Very rarely development of antibodies to hamster protein with related hypersensitivity reactions has been observed.

Development of neutralising antibodies (inhibitors) may occur in patients with haemophilia A treated with factor VIII, including with Esperoct. If such inhibitors occur, the condition will manifest itself as an insufficient clinical response. In such cases, it is recommended that a specialised haemophilia centre is contacted.

Tabulated list of adverse reactions

The frequencies of adverse reactions as observed in 270 unique subjects across five prospective, multi-centre clinical studies in previously treated patients (PTPs) with severe haemophilia A (<1% endogenous factor VIII activity) and no history of inhibitors are listed in table 3. The categories of adverse reactions presented in table 3 is according to the MedDRA system organ classification (SOC and Preferred Term Level).

Frequencies have been evaluated according to the following convention: very common (≥1/10), common (≥1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥1/10,000 to <1,000), very rare (<1/10,000); not known (cannot be estimated from the available data).

Table 3 Frequency of adverse reactions for PTPs*

MedDRA System Organ Class	Adverse reactions	Frequency
Blood and lymphatic system disorders	Factor VIII inhibition	Uncommon (PTPs)**
Immune system disorders	Hypersensitivity	Uncommon
Skin and subcutaneous tissue disorders	Rash Erythema	Common

	Pruritus	
General disorders and administration sites conditions	Injection site reactions***	Common
Investigations	Coagulation factor VIII level decreased	Unknown****

* PTPs: Previously-treated patients.
** Frequency is based on studies with all factor VIII products which included patients with severe haemophilia A.
*** Preferred terms included in injection site reactions: Injection site reaction, Vessel puncture site haematoma, Infusion site reaction, Injection site erythema, Injection site rash, Vessel puncture site pain, and Injection site swelling.
**** Based on post marketing reports.

Description of selected adverse reactions

Factor VIII inhibitors
One confirmed case of factor VIII inhibitor occurred in an 18 year-old previously treated patient on prophylactic treatment with Esperoct. The patient had a factor VIII gene intron 22 inversion and was at a high risk of developing factor VIII inhibitors.
There is no indication of an increased risk of factor VIII inhibitor development with treatment of Esperoct as compared to other factor VIII products.

Anti-drug antibodies
There was one case of persistent anti-drug antibodies concomitant with the confirmed case of factor VIII inhibitors (see Factor VIII inhibitors). Three patients had transiently positive test results for anti-drug antibodies after administration of Esperoct but no correlation with adverse events could be established.

Anti-PEG antibodies
During the clinical trial programme, thirty-two patients had pre-existing anti-PEG antibodies before administration of Esperoct. Twenty of the 32 patients were negative for anti-PEG antibodies post administration of Esperoct. Eleven patients developed transient low titre anti-PEG antibodies. No correlation with adverse events could be established.
From post-marketing reporting, occurrence of anti-PEG-antibodies has also been observed at time of switching to Esperoct. In some patients anti-PEG antibodies may have been associated with lower than expected level of FVIII activity.

Paediatric population

In the safety profile of Esperoct®, no difference was detected between previously treated children and adolescents and adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form http://sideeffects.health.gov.il which refer the user to an online adverse reaction reporting form, or by entering the following link: http://sideeffects.health.gov.il.

4.9 Overdose

No symptoms of overdose with recombinant coagulation factor VIII have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antihemorrhagics, blood coagulation factor VIII, ATC code: B02BD02.

Mechanism of action

Turoctocog alfa pegol is a purified recombinant human factor VIII (rFVIII) product with a 40 kDa polyethylene-glycol (PEG) conjugated to the protein. The PEG is attached to the O-linked glycan in the truncated B-domain of rFVIII (turoctocog alfa). The mechanism of action of turoctocog alfa pegol is based on the replacement of the deficient or absent factor VIII in patients with haemophilia A.
When turoctocog alfa pegol is activated by thrombin at the site of injury, the B-domain containing the PEG moiety and the a3-region are cleaved off, thus generating activated recombinant factor VIII (rFVIIIa) which is similar in structure to native factor VIIIa.
The factor VIII/von Willebrand factor complex consists of two molecules (factor VIII and von Willebrand factor) with different physiological functions. When injected into a haemophiliac patient, factor VIII binds to von Willebrand factor in the patient's circulation. Activated factor VIII acts as a cofactor for activated factor IX, accelerating the conversion of factor X to activated factor X.
Activated factor X converts prothrombin into thrombin. Thrombin then converts fibrinogen into fibrin and a clot can be formed. Haemophilia A is a sex-linked hereditary disorder of blood coagulation due to decreased levels of factor VIII:C and results in profuse bleeding into joints, muscles or internal organs, either spontaneously or as results of accidental or surgical trauma. By factor VIII replacement therapy the plasma levels of factor VIII are increased, thereby enabling a temporary correction of the factor deficiency and correction of the bleeding tendencies.

Clinical efficacy during prophylaxis and treatment of bleeding episodes

The clinical efficacy of Esperoct for prophylaxis and treatment of bleeds was investigated in five prospective, multi-centre clinical studies in 270 previously treated patients (PTPs) with severe haemophilia A.
The haemostatic effect was confirmed in adults/adolescents and in children.

Prophylaxis in adults/adolescents

The efficacy of Esperoct for prophylaxis and treatment of bleeds was evaluated in an open-label, non-controlled trial in adolescents and adult patients with severe haemophilia A ages 12 years and above. The prophylactic effect of Esperoct was demonstrated with a dosing at 50 IU per kg body weight every 4 days or every 3–4 days (twice weekly) in 175 patients. The median annualized bleeding rate (ABR) in adults and adolescents receiving Esperoct was 1.18 (Interquartile range IQR: 0.00;4.25), whereas the spontaneous ABR was 0.00 (IQR: 0.00;1.82), traumatic ABR was 0.00 (IQR: 0.00;1.74) and joint ABR was 0.85 (IQR: 0.00;2.84). When including imputations, (replacing missing data for withdrawn patients with a substituted value) the estimated mean ABR for all bleeds was 3.70 (95% CI: 2.94;4.66). Of

the 175 adults/adolescents on prophylaxis, 70 (40%) did not have any bleeds. The mean annual consumption for prophylaxis was 4641 IU/kg.

Of note, annualized bleeding rate (ABR) is not comparable between different factor concentrates and between different clinical studies.

Adults/adolescents who had a low bleeding rate of 0-2 bleeding episodes during the last 6 months and had obtained at least 50 doses of Esperoct had the option of being randomised to prophylaxis treatment every 7 days (75 IU/kg every 7 days) or every 4 days (50 IU/kg every 4 days). A total of 55 of the 120 eligible patients chose to be randomised (17 to the every 4 days dosing and 38 to the 75 IU every 7 days). The ABR for randomised patients was 1.77 (0.59; 5.32) for treatment every 4 days and 3.57 (2.13; 6.00) for once weekly prophylaxis. Nine of these patients reverted back to prophylaxis every 4 days during the randomised study phase. Overall, including all extensions parts, 31 of 61 patients on every 7 days prophylaxis switched back to every 4 days treatment.

Prophylaxis in children (below 12 years)

The efficacy and safety of Esperoct for prophylaxis treatment of bleeds were evaluated in an open-label, single-arm, non-controlled trial in 68 children below 12 years with severe haemophilia A.
The prophylactic effect of Esperoct was demonstrated with a dosing at 60 IU per kg body weight (50-75 IU/kg) twice weekly. The median and estimated mean annualised bleeding rate in children below 12 years receiving Esperoct twice weekly was 1.95 and 2.13 (95% CI: 1.48;3.06), whereas the spontaneous ABR was 0.00 and 0.58 (95% CI: 0.24;1.40), traumatic ABR was 0.00 and 1.52 (95% CI: 1.07;2.17) and joint ABR was 0.00 and 1.03 (95% CI: 0.59;1.81), respectively. Of the 68 children below 12 years on prophylaxis, 29 (42.6%) did not have any bleeds.
The mean annual consumption for prophylaxis was 6475 IU/kg.

Clinical efficacy of Esperoct in treatment of bleeding episodes and during on-demand treatment

The efficacy of Esperoct in the treatment of bleeding episodes was demonstrated in all age groups.
The vast majority of bleeds treated with Esperoct were of mild/moderate severity.
The overall success rate for the treatment of bleeds was 87.7% and 94.4% of all bleeds treated with 1-2 injections.

In 12 patients above 18 years of age, 1,126 bleedings were treated among patients receiving on-demand treatment with an average treatment dose of 38.1 IU/kg with a mean annual consumption of 1457 IU/kg. Of the total 1,126 bleeds, 86.9% were effectively treated with 1 injection and 96.8% were effectively treated with 1-2 injections of Esperoct.

Clinical efficacy of Esperoct during major surgery

Esperoct was effective in maintaining haemostasis during major surgery with a success rate of 95.6% in all major surgeries performed (43 out of 45 had the effect rated as ‘excellent‘ or ‘good‘).

5.2 Pharmacokinetic properties

In total, 129 single-dose pharmacokinetic (PK) profiles of Esperoct were evaluated in 86 patients (including 24 paediatric patients of 0 to below 12 years).

All pharmacokinetic studies with Esperoct were conducted in previously treated patients with severe haemophilia A (factor VIII <1%). Patients received a single dose of 50 IU/kg, and blood samples were collected prior to dosing and at multiple time points up to 96 hours after dosing.

The half-life of Esperoct was 1.6 fold longer compared to unmodified factor VIII products in adults.

Pharmacokinetic parameters

A total of 108 single dose pharmacokinetic profiles at 50 IU/kg Esperoct were evaluated in 69 patients. The single dose pharmacokinetic parameters are comparable between young children (0 to below 6 years) and older children (6 to below 12 years), and between adolescents (12 to17 years) and adults (18 years and above).
As expected incremental recovery appeared to be lower while body weight adjusted clearance appeared to be higher in children compared to adults and adolescents. In general, there was a trend of increasing incremental recovery and decreasing clearance (mL/h/kg) with age. This corresponds to a higher volume of distribution per kilo body weight in children compared to adults (table 4).
The single dose pharmacokinetic parameters determined after 28 weeks of prophylactic treatment with Esperoct were consistent with the initial pharmacokinetic parameters.

Single-dose pharmacokinetic parameters of Esperoct are listed in table 4.

Table 4 Single-dose pharmacokinetic parameters of Esperoct 50 IU/kg in children, adolescents and adults by age using the chromogenic assay (geometric mean [CV%])

PK Parameter N=No. of patients	0 to below 6 years N=13	6 to below 12 years N=11	12 to below18 years N=3	18 years and above N=42
Number of profiles	13	11	5	79
IR (IU/dL) per (IU/kg)a	1.80 (29)	1.99 (25)	2.79 (12)	2.63 (22)
Maximum factor VIII activity (IU/dL)[a]	101.2 (28)	119.6 (25)	133.2 (9)	134.4 (23)
t1/2 (hours)	13.6 (20)	14.2 (26)	15.8 (43)	19.9 (34)
AUCinf (IU*hour/dL)	2147 (47)	2503 (42)	3100 (44)	3686 (35)
CL (mL/hour/kg)	2.6 (45)	2.4 (40)	1.5 (43)	1.4 (32)
Vss (mL/kg)	44.2 (34)	41.2 (25)	33.4 (10)	37.7 (27)
MRT (hours)	17.0 (22)	17.3 (31)	21.7 (45)	25.2 (29)[b]

Abbreviations: AUC = area under the factor VIII activity time profile; t1/2 = terminal half-life; MRT = mean residence time; CL = clearance;
Vss = volume of distribution at steady–state; IR = Incremental recovery.

[a] Incremental recovery and factor VIII were assessed 30 min post-dosing for patients 12 years and above and 60 min post-dosing (first sample) for children below12 years.
[b] Calculation based on 67 profiles.
The mean trough plasma factor VIII activity levels at steady–state during prophylactic treatment with Esperoct dosed with 50 IU/kg every 4 days is 3.0 IU/dL (95% CI: 2.6;3.4) in patients 12 years and above.
For patients under 12, who received 60 IU/kg (50 – 75 IU/kg) twice weekly, the mean steady-state factor VIII plasma activity level before administration during prophylactic treatment was 1.5 IU/dl (95% CI: 1.2; 1.9).

5.3 Preclinical safety data

Non-clinical data reveal no special concern for humans based on conventional studies of safety pharmacology and repeated dose toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder

Sodium chloride
Sucrose
L-Histidine
Calcium chloride dihydrate
Polysorbate 80
L-Methionine
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)

Solvent

Sodium chloride
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products or reconstituted with injection solutions other than the provided sodium chloride solvent.

The reconstituted product should not be administered in the same tubing or container with other medicinal products.

6.3 Shelf life

The expiry date of the product is indicated on the package.
Unopened vial (before reconstitution):

36 months when stored in a refrigerator (2°C – 8°C).

During the shelf life the product may be kept:

- at room temperature (≤30ºC) for a single period no longer than 12 months

or

- above room temperature (>30°C up to 40°C) for a single period no longer than 3 months

Once the product has been stored outside of the refrigerator, the product must not be returned for storage in the refrigerator.

Record the beginning of storage outside refrigerator and the storage temperature in the space provided on the carton.

After reconstitution

Chemical and physical in-use stability have been demonstrated for:

- 24 hours when stored in a refrigerator (2°C - 8°C) or
- 4 hours at ≤30ºC or
- 1 hour between >30ºC and 40ºC. only if the product was stored above room temperature (>30ºC up to 40ºC) before reconstitution for no longer than 3 months.

From a microbiological point of view, the product should be used immediately after reconstitution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the users and would normally not be recommended for longer than as stated above, unless reconstitution has taken place in controlled and validated aseptic conditions.

The reconstituted solution should be stored in the vial.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Store in the original package in order to protect from light.

For storage at room temperature (≤30ºC) or up to 40ºC and storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Each pack of Esperoct contains:

- 1 glass vial (type I) with powder closed with a chlorobutyl rubber stopper, an aluminium seal with a plastic snap-off cap
- 1 sterile vial adapter for reconstitution
- 1 pre-filled syringe of 4 mL solvent with backstop (polypropylene), a rubber plunger (bromobutyl) and a rubber tip cap (bromobutyl)
- 1 plunger rod (polypropylene).

6.6 Special precautions for disposal and other handling

Esperoct is to be administered intravenously after reconstitution of the powder with the solvent supplied in the syringe. After reconstitution the solution appears as a clear and colourless liquid free of visible particles. The reconstituted medicinal product should be inspected visually for particulate matter and discolouration prior to administration. The solution should be clear and colourless. Do not use solutions that are cloudy or have deposits.

For instructions on reconstitution of the medicinal product before administration, see the package leaflet.

The rate of administration should be determined by the patient's comfort level over approximately 2 minutes.

An infusion set (butterfly needle with tubing), sterile alcohol swabs, gauze pads and plasters will also be needed. These devices are not included in the Esperoct package.

Always use an aseptic technique.

Disposal

After the injection, safely dispose of the syringe with the infusion set and the vial with the vial adapter.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novo Nordisk Ltd.,
1 Atir Yeda St.,
Kfar-Saba 4464301

8. MANUFACTURER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsvaerd
Denmark

9. REGISTRATION NUMBER

172-44-37440-00

Approved by MOH on March 2023